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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,404	ARNDT ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/13/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *7-14,16-18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) *1-6, 15, 19, and 22* is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 06/13/2006, is acknowledged.

Claims 1-3, 5, 17, and 19 have been amended.
Claim 22 has been added.
Claims 1-22 are pending.

Claims 7-14, 16-18, 20, and 21 have been withdrawn from further consideration by the Examiner under 37 C.F.R. 1.142(b) as being drawn to nonelected invention.

Claims 1-6, 15, 19, and 22, read on originally elected invention of an Fv antibody construct having binding site for CD16 and CD30, are currently under consideration.

2. Applicant's asserts that German references AC, AD, cited on IDS, filed 06/07/2002, corresponds to US Patents 5,643,795, 6,294,167, respectively, and reference the German reference AE relates to a monovalent anti-CD30 single-chain Fv. Therefore, references AC, AD, and AE have been considered.

3. The text of those Sections of Title 35 U.S.C. not included in this Action can be found in a prior Action.

This Office Action will be in response to applicant's amendment, filed 06/13/2006.

The rejection of record can be found in the previous Office Action, mailed 03/13/2006.

4. Claim 22 is rejected under **35 U.S.C. 112, second paragraph,** as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite in the recitation of "a more intense lysis" because "a more intense lysis" is a relative phrase which renders the claim indefinite. The phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

5. Newly submitted claim 22 is rejected under **35 U.S.C. 112, first paragraph,** as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the antibody bimAbHRS-3/A9 (DSM ACC2124) is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridoma, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

It is noted that applicant has indicated that the antibody bimAbHRS-3/A9 (DSM ACC2124) was described in US Patent 5,643,795 (see page 2 of the amended specification).

However, biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question from a given depository prior to and after the filing date of the application does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public. Applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from the depository, nor is there any evidence as to the depository's policy regarding the material if a patent would be granted. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. In the absence of evidence that the antibody bimAbHRS-3/A9 (DSM ACC2124) is readily available to the public and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, the rejection under enablement requirements of 35 USC 112, first paragraph, is set forth herein.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicant or someone associated with the patent owner who is in a position to make such assurances, or statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of the deposit, 5 years after the last request for a sample, or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Applicant is required to make the record clear exactly what is the scope of the instantly claimed bimAbHRS-3/A9 (DSM ACC2124) and whether applicant has satisfied the deposit requirements under 35 USC 112, first paragraph, for the claimed bimAbHRS-3/A9 (DSM ACC2124).

6. Claims 1-6, 15, 19, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a *Written Description*, New Matter rejection.

The phrases "inducing regression of Hodgkin's disease in vivo" recited in claims 1-6, 15, 19, and 22 and "CD30 carrying cells" recited in claim 22 are not supported by the original disclosure or claim as filed.

Applicant's amendment, filed 06/13/2006, has directed the supports of these phrases to page 2 of the instant specification.

However, the specification as-filed does not provide sufficient written description of the above-mentioned "limitations". The specification does not provide sufficient support for "inducing regression of Hodgkin's disease in vivo" and "CD30 carrying cells". The specification only discloses tumor cells from Hodgkin's disease and the claimed Fv antibody construct activate natural killer cells in vitro and in vivo (e.g. see pages 2 and 10-11 of the instant specification); the instant claims now recite "inducing regression of Hodgkin's disease in vivo" and "CD30 carrying cells", which were not clearly disclosed in the specification. Therefore, the claims represent a departure from the specification and claims originally filed. Applicant's reliance on generic disclosure (e.g. tumor cells and activate natural killer cells in vitro and in vivo) and possibly a single or limited species do not provide sufficient direction and guidance to the features currently claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679 683 (CCPA 1972) and MPEP 2163.05.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduces new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02, 2163.05-06 and 2173.05 (i).

7. Claims 1-6, 15, 19 and 22 are rejected under **35 U.S.C. 102(a)** as being anticipated by Arndt et al. (Blood, 1999. 94; 8:2562-2568. Reference AI on IDS) for reasons of record set forth in the previous Office Action.

Arndt et al. teaches that diabody binding to both CD16 and CD30 is capable of inducing more lysis of CD30 tumor cells in vitro than the CD16/CD30 bispecific antibody (see entire document, particularly Results on page 2564-2565).

Therefore, the reference teachings anticipate the claimed invention.

Applicant asserts that the English translation of the priority document GERMANY 199 37 264 will be submitted.

The rejection is maintained until the English translation of the priority document GERMANY 199 37 264 is provided and the written support and enablement under 35 U.S.C 112, first paragraph in the foreign priority document is determined.

8. Claims 1-5, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hartmann et al. (Blood. 1997, 89;6:2042-2047) (see entire document) for reasons of record set forth in the previous Office Action.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant argues that Hartmann et al. do not teach ani-CD16/CD30 single-chain antibody.

This is not found persuasive for following reasons:

Contrary to applicant's argument, Hartmann et al. (Blood. 1997, 89;6:2042-2047) clearly teach that the side effects such as HAMAs in the anti-CD16/CD30 bispecific antibody treatment can be resolved by using less immunogenic bispecific single chain antibody or diabodies (see entire document, particularly pages 2042-2046).

It is noted that a prior art reference must be considered in its entirety.

The teachings of Hartmann et al, when considered in its entirety, e.g. the use of ati-CD16/CD30 bispecific antibody in treating human patients and the conclusion that single chain or diabodies without Fc region can resolve the side effects such as HAMAs, clearly anticipate the claimed invention.

Therefore, the reference teachings anticipate the claimed invention.

9. Claims 1-6, 15 19, and 22 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Hartmann et al **(Leukemia and Lymphoma. 1998, 31:385-392. Reference AG on IDS)** in view of Holliger et al. (PNAS. 1993, 93:6444-6448) for reasons of record set forth in the previous Office Action.

Applicant's arguments have been fully considered but have not been found persuasive.

It is noted that applicant's arguments regarding Hartmann et al. (Blood. 1997, 89;6:2042-2047) and Arndt et al. are directed to the references that are not cited in the rejection of record under 35 U.S.C. 103 (a).

Applicant argues that Holliger et al. do not specifically teach a diabody having binding sites for CD16 and CD30; and further, Holliger et al. do not teach any therapeutic (e.g. cytotoxic) diabodies. Furthermore, applicant argues that neither Hartmann et al. nor Holliger et al. provide any evidence suggesting that anti-CD16/CD30 Fv antibody would be therapeutically effective.

Moreover, applicant argues that diabodies are smaller than IgG-antibodies, thus diabodies are cleared much faster from serum than IgG antibodies, and Arndt et al. reports that the half-life of diabodies was about 6h, whereas the half-life of IgG antibodies was about 107h according to Hartmann et al. Therefore, the prior art teachings of the diabodies would not be sufficiently cytotoxic and capable to elicit a therapeutic effect due to their short half-life.

This is not found persuasive for the following reasons:

Contrary to applicant's arguments, Hartmann et al. (Leukemia and Lymphoma. 1998, 31:385-392. Reference AG on IDS) that has been applied in the rejection under 35 U.S.C. 1023(a) teach bispecific anti-CD16/CD30 antibody can be used for immunotherapy for tumor-specific recruitment and activation of immunologic effector cells (see entire document, particularly pages 385-390).

Regarding the reasons of combining the teachings of Hartmann et al. and Holliger et al., it is noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01.

Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA). In re Burckel is cited in MPEP 716.02.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

Here, given that antigen binding fragments can be preferable to complete antibodies because the Fc region of antibodies can lead to unwanted targeting to cells expressing Fc receptors (see Holliger et al. page 6444, in particular) and that the bispecific anti-CD16/CD30 antibody binds CD30 expressed on Hodgkin and Reed-Sternberg cells and CD16 on NK cells leading to specific tumor cell killing (see Hartmann et al. Leukemia and Lymphoma. 1998, 31:385-392. Reference AG on IDS), it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of the references to reduce or eliminate the side effects associated with non-specific binding between the Fc region of bi-specific anti-CD16/CD30 antibody to the Fc receptors.

In addition, in addressing applicant's arguments regarding Hartmann et al. (Blood. 1997, 89;6:2042-2047) that is not cited in the rejection of record under 35 U.S.C. 103, it is noted that the serum half-life for whole IgG antibodies in humans are six-fourty-eight (6-48) hours and saturation of circulating NK cells with ani-CD16/CD30 bispecific antibody HRS-3/A9 peaked at six (6) hours (e.g. see left column on page 2045). Thus, the therapeutic effect of the diabody would not be compromised by its 6 hours of half-life.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Upon further consideration as well as applicant's amendments, the previous Objections and rejections under 35 U.S.C. 112, first paragraph and second paragraph have been withdrawn.

11. ***Conclusion: no claim is allowed.***

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
August 14, 2006

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1600
8/18/06